Remarks

Claims 9, 11, 12, 14, 48 and 51 were pending. No claims are cancelled or added. Therefore, claims 9, 11, 12, 14, 48 and 51 are still pending.

Support for claim 9 can be found in Experiments 1 and 2 in the specification.

No new matter is introduced by this amendment, and no amendments are made to distinguish prior art.

Summary of Telephone Interview with Examiner

Applicants thank Examiner Nguyen for the courtesy of a telephone interview with Applicants' representative Sheree Lynn Rybak, Ph.D. on March 6, 2007. During this interview, the 35 U.S.C. § 103(a) and § 112 rejections were discussed.

Examiner Nguyen agreed that amending the phrase "few weeks" to "three to five weeks" would likely overcome the 35 U.S.C. § 112, second paragraph rejection.

Examiner Nguyen agreed that the dosage in claim 9 was not useful in overcoming the 35 U.S.C. § 103 rejections. Therefore, Applicants' representative suggested that it would be deleted.

Agreement was not reached on the 35 U.S.C. § 103 rejection. Applicants' representative noted that the cited Stratford-Perricaudet *et al.* article disclosed different results depending on the mode of administration (i.m. and i.v.), and that one of the cited Denham *et al.* references (*J. Gastrointest. Surg.* 2:95, 1989) disclosed different results depending on mode of administration (i.p. and directly into the pancreas). Applicants' representative explained that this demonstrates that the results achieved using a particular mode of administration is not predictable. Examiner Nguyen agreed to re-consider the rejection in view of these teachings.

35 U.S.C. § 112, second paragraph

Claims 9, 11, 12, 14, 48, and 51 are rejected under 35 U.S.C. § 112, second paragraph. Applicants request reconsideration. Claim 9 is amended to recite "three to five weeks." Support for this amendment can be found in Examples 1 and 2 of the application.

In view of the amendment to claim 9, Applicants request that the 35 U.S.C. § 112, second paragraph rejection be withdrawn.

35 U.S.C. § 103(a)

Claims 9, 11, 12, 14, 48 and 51 are rejected under 35 U.S.C. § 103(a) as unpatentable over Morishita *et al.* (EP 0847757) in view of an article from the Japan Financial Times (December 14, 1998). Applicants disagree and request reconsideration.

It is asserted on page 7 of the Office action that Stratford-Perricaudet *et al.* demonstrates long-term *in vivo* gene transfer, and that expression was detected in muscle tissues 10-12 months post-injection. However, the Stratford-Perricaudet *et al.* article also teaches that transgene expression is dependent on the mode of administration. For example, the results described on page 7 of the Office action were achieved using intravenous injection of the vector. However, on page 627 (column 2, 3rd full paragraph) Stratford-Perricaudet *et al.* states that when intramuscular injection was used, infection was circumscribed to the point of injection at 21 days after injection, and long-term expression was not examined. Based on the teachings of the cited Stratford-Perricaudet *et al.* article, one skilled in the art would conclude that effective gene expression will depend on the mode of administration. Specifically, intramuscular injection is taught by Stratford-Perricaudet *et al.* to be less effective than intravenous injection. Therefore, it would not be obvious to one skilled in the art based on the teachings of Stratford-Perricaudet *et al.* that intramuscular injection could be effective to deliver a transgene to a distant affected site and treat target diseases even if the transgene expression lasted 21 days.

It is asserted on page 8 of the Office action that the two Denham *et al.* documents demonstrate expression for up to 2 weeks. However, the Denham *et al.* documents (specifically the *J. Gastrointest. Surg.* article) teach that mode of administration can affect transgene expression and the response in the treated subject. For example, the results described on page 8 of the Office action were achieved using intraperitoneal injection of the liposomes and plasmid. However, on page 100 (column 1, 1st full paragraph) Denham *et al.* states that when the pancreas was injected directly, undesirable pancreatic inflammation and tissue destruction were observed. Based on the teachings of the cited Denham *et al.* (*J. Gastrointest. Surg.*) article, one skilled in

the art would conclude that the combination of desirable gene expression and absence (or reduction) of serious undesirable side effects, will depend on the mode of administration. In addition, one skilled in the art would have concluded that transgene expression depends on target organs and administration routes. Therefore, it would not be obvious to one skilled in the art based on the teachings of Denham *et al.* that intramuscular injection could be effective to deliver a transgene to an affected site and treat target diseases, in the absence (or reduction) of undesirable side effects.

In summary, Morishita *et al.* (EP 0847757) and the Japan Financial Times article do not teach or suggest administration of an HGF gene into skeletal muscle once every 3-5 weeks. Further, in view of the cited Stratford-Perricaudet *et al.* and Denham *et al.* articles, it would not be obvious to one skilled in the art that expression of an HGF gene can treat diabetic ischemic diseases by intramuscular injection every 3-5 weeks. Therefore, Applicants request that the 35 U.S.C. §103(a) rejection be withdrawn.

Double Patenting

Claims 9, 11-12, 14, 48, and 51 are rejected on the ground of non-statutory obviousness-type double patenting. Applicants disagree and request reconsideration, for the reasons described above.

If necessary, Applicants will consider filing a terminal disclaimer, but prefer to wait until the 35 U.S.C. §103(a) rejection is resolved.

If there are any questions regarding this response, the Examiner is invited to telephone the undersigned.

Respectfully submitted,

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